Message

From: Williams, Antony [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=959E02B5A0DA419A9D749469DFE05C34-WILLIAMS, A]
Sent: 7/2/2019 5:55:25 PM
To: Sun, Meng@OEHHA [meng.sun@oehha.ca.gov]; Paul-Friedman, Katie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9de6209426a941908301318615f5507b-Paul-Friedm]
CC: Nathalie.Pham@oehha.ca.gov [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd2e1b496eb64fee863efc2d8dae84b6-Nathalie.Ph]
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Glad to be of assistance. Please reach out with other questions as necessary. Best wishes.

Antony J. Williams
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From: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Sent: Tuesday, July 2, 2019 12:27 PM
To: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>; Williams, Antony <Williams.Antony@epa.gov>
Cc: Nathalie.Pham@oehha.ca.gov
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Katie and Tony,

Thank you both very much for the publication and explanation. Now we have a better understanding for the cytotoxicity threshold. I'd like to introduce my colleague Nathalie Pham. She also uses ToxCast data frequently and may reach out to you for technical questions. We really appreciate your help with our use of the Chemicals Dashboard.

Best,
Meng

From: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>
Sent: Monday, July 1, 2019 6:32 PM
To: Williams, Antony <Williams.Antony@epa.gov>; Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Meng and Tony,

Yes, the publication that Tony referenced provides a detailed description of the calculation. Currently there are 88 cytotoxicity assays that can be included in the cytotoxicity threshold computation (though not all chemicals have been screened in all 88). The cytotoxicity threshold that appears on the Dashboard is actually the lower bound on the prediction of the median cytotoxicity, so it will appear lower than many of the hits. We do not currently filter out any data; the cytotoxicity threshold is truly more for context in terms of identifying activity that looks like it occurs "specifically," i.e. less likely to be confounded by cytotoxicity. Obviously any filtering applied by a user should be context specific. I'm happy to dive deeper into this and the computation itself with you if you have some more specific questions. Please reach out anytime.

Kind regards,
Katie

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From: Williams, Antony
Sent: Monday, July 1, 2019 8:39 PM
To: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Cc: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Meng,

Thank you for your email. While I can take a poke at a number of your questions I believe that the publication at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6280881/ will cover a number of your questions. My colleague Katie Paul-Friedman is far more familiar with the data and details of determining the cytotoxicity limits and I have cc'ed her on this email as her responses will offer way more detail than I can provide. Best wishes.

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From: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Sent: Monday, July 1, 2019 2:07 PM
To: Williams, Antony <Williams.Antony@epa.gov>
Subject: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Tony,

I hope you are doing well. This is Meng from OEHHA at Cal/EPA. My colleagues and I have some additional questions regarding the Chemicals Dashboard. It is such a great resource and we are trying to make the best use out of it.

Our questions are: how do you calculate the single cytotoxicity cutoff that appears on the "chemical activity summary" chart? Is it based on a combination of the variability assay results? Do you use this cutoff to filter out any assays? For example, the cytotoxicity cutoff for 4-aminophenol is very low (8.22 µM) and a lot of the current "positives" have an AC50 of higher than 20 or even 50 µM. When we checked individual variability assays, the AC50s look more comparable

to the AC50s of the "real signal" such as ER inhibition. We are trying to tease out the cytotoxic effect from specific receptor antagonism, and wonder if we can use this cutoff or should check individually paired variability assay results.

Thank you very much!

Meng

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